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The Government of the United States of America
as represented by the Secretary of the
Department of Health and Human Services

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<141> 2000-03-24

<151> 1999-03-25

<160> 32

<170> PatentIn Ver. 2.1

 $\langle 210 \rangle$ 1

$\langle 211 \rangle$ 1343

<212> DNA

<213> Homo sapiens

 $\langle 220 \rangle$

<221> CDS

 $\langle 222 \rangle \quad (284) \dots (781)$

<223> human growth arrest and DNA-damage-inducible
protein (GADD45)

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cqgggagcga qcgaqcaagc aaqgcqggag gqgtggccgg agctgcggcg gctggcacag 120

gaggaggaqc ccgggcgggc gaggggcggc cggagagcgc cagggcctga gctgccggaq 180

cggcgcctgt gagtgaqtgc agaaagcagg cggccgcgcg ctagccgtgg caggagcagc 240

ccgcacgcgcg cgctctctcc ctgggcgcacc tgcagtttgc aat atg act ttg gag 295
Met Thr Leu Glu
1

gaa ttc tcg gct gga gag cag aag acc gaa agg atg gat aag gtg ggg 343
Glu Phe Ser Ala Gly Glu Gln Lys Thr Glu Arg Met Asp Lys Val Gly
5 10 15 20

gat gcc ctg gag gaa gtg ctc agc aaa gcc ctg agt cag cgc acg atc 391
Asp Ala Leu Glu Glu Val Leu Ser Lys Ala Leu Ser Gln Arg Thr Ile
25 30 35

act gtc ggg gtg tac gaa gcg gcc aag ctg ctc aac gtc gac ccc gat 439
Thr Val Gly Val Tyr Glu Ala Ala Lys Leu Leu Asn Val Asp Pro Asp
40 45 50

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aac gtg gtg ttg tgc ctg ctg gcg gcg gac gag gac gac gac aga gat 487
Asn Val Val Leu Cys Leu Leu Ala Ala Asp Glu Asp Asp Asp Arg Asp
      55                      60                      65

gtg gct ctg cag atc cac ttc acc ctg atc cag gcg ttt tgc tgc gag 535
Val Ala Leu Gln Ile His Phe Thr Leu Ile Gln Ala Phe Cys Cys Glu
      70                      75                      80

aac gac atc aac atc ctg cgc gtc agc aac ccg ggc cgg ctg gcg gag 583
Asn Asp Ile Asn Ile Leu Arg Val Ser Asn Pro Gly Arg Leu Ala Glu
      85                      90                      95                      100

ctc ctg ctc ttg gag acc gac gct ggc ccc gcg gcg agc gag ggc gcc 631
Leu Leu Leu Leu Glu Thr Asp Ala Gly Pro Ala Ala Ser Glu Gly Ala
      105                      110                      115

gag cag ccc ccg gac ctg cac tgc gtg ctg gtg acg aat cca cat tca 679
Glu Gln Pro Pro Asp Leu His Cys Val Leu Val Thr Asn Pro His Ser
      120                      125                      130

tct caa tgg aag gat cct gcc tta agt caa ctt att tgt ttt tgc cgg 727
Ser Gln Trp Lys Asp Pro Ala Leu Ser Gln Leu Ile Cys Phe Cys Arg
      135                      140                      145

gaa agt cgc tac atg gat caa tgg gtt cca gtg att aat ctc cct gaa 775
Glu Ser Arg Tyr Met Asp Gln Trp Val Pro Val Ile Asn Leu Pro Glu
      150                      155                      160

cgg tga tggcatctga atgaaaataa ctgaacccaaa ttgcactgaa gtttttgaaa 831
Arg
165

tacctttgta gttactcaag cagttactcc ctacactgat gcaaggatta cagaaactga 891

tgccaagggg ctgagtgagt tcaactacat gttctggggg cccggagata gatgactttg 951

cagatggaaa gaggtgaaaa tgaagaagga agctgtgttg aaacagaaaa ataagtcaaa 1011

aggaacaaaa attacaaaga accatgcagg aaggaaaact atgtattaat ttagaatggt 1071

tgagttacat taaaataaac caaatatggt aaagtttaag tgtgcagcca tagtttgggt 1131

atTTTTggtt tatatgccct caagtaaaag aaaagccgaa aggggttaatc atatttgaaa 1191

accatatttt attgtatttt gatgagatat taaattctca aagttttatt ataaattcta 1251

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tacaataaac tggatatgaat aattgcatca tt 1343

<210> 2
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<213> Homo sapiens

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 Gln Arg Thr Ile Thr Val Gly Val Tyr Glu Ala Ala Lys Leu Leu Asn
 35 40 45
 Val Asp Pro Asp Asn Val Val Leu Cys Leu Leu Ala Ala Asp Glu Asp
 50 55 60
 Asp Asp Arg Asp Val Ala Leu Gln Ile His Phe Thr Leu Ile Gln Ala
 65 70 75 80
 Phe Cys Cys Glu Asn Asp Ile Asn Ile Leu Arg Val Ser Asn Pro Gly
 85 90 95
 Arg Leu Ala Glu Leu Leu Leu Leu Glu Thr Asp Ala Gly Pro Ala Ala
 100 105 110
 Ser Glu Gly Ala Glu Gln Pro Pro Asp Leu His Cys Val Leu Val Thr
 115 120 125
 Asn Pro His Ser Ser Gln Trp Lys Asp Pro Ala Leu Ser Gln Leu Ile
 130 135 140
 Cys Phe Cys Arg Glu Ser Arg Tyr Met Asp Gln Trp Val Pro Val Ile
 145 150 155 160
 Asn Leu Pro Glu Arg
 165

<210> 3
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 <212> DNA
 <213> Artificial Sequence

<220>
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<400> 3
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<210> 4
 <211> 24
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:PCR
 amplification primer

<400> 4
 catcaccgtt caggagatt aatc

24

<210> 5
 <211> 6
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:GADD45
 subsequence acidic motif amino acid residues
 62-67; exemplary peptide inhibiting GADD45-related
 dissociation of Cdc2/cyclin B1 complexes

<400> 5
 Asp Glu Asp Asp Asp Arg
 1 5

<210> 6
 <211> 160
 <212> PRT
 <213> Homo sapiens

<220>
 <223> human growth arrest and DNA-damage-inducible
 protein (hGADD45beta)

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 1 5 10 15
 Gln Thr Val Thr Ala Ala Val Glu Glu Leu Leu Val Ala Ala Gln Arg
 20 25 30
 Gln Asp Arg Leu Thr Val Gly Val Tyr Glu Ser Ala Lys Leu Met Asn
 35 40 45
 Val Asp Pro Asp Ser Val Val Leu Cys Leu Leu Ala Ile Asp Glu Glu
 50 55 60
 Glu Glu Asp Asp Ile Ala Leu Gln Ile His Phe Thr Leu Ile Gln Ser
 65 70 75 80
 Phe Cys Cys Asp Asn Asp Ile Asn Ile Val Arg Val Ser Gly Met Gln
 85 90 95
 Arg Leu Ala Gln Leu Leu Gly Glu Pro Ala Glu Thr Gln Gly Thr Thr
 100 105 110
 Glu Ala Arg Asp Leu His Cys Leu Leu Val Thr Asn Pro His Thr Asp
 115 120 125
 Ala Trp Lys Ser His Gly Leu Val Glu Val Ala Ser Tyr Cys Glu Glu
 130 135 140
 Ser Arg Gly Asn Asn Gln Trp Val Pro Tyr Ile Ser Leu Gln Glu Arg
 145 150 155 160

<210> 7
 <211> 159
 <212> PRT
 <213> Homo sapiens

<220>
 <223> human growth arrest and DNA-damage-inducible
 protein (hGADD45gamma)

<400> 7
 Met Thr Leu Glu Glu Val Arg Gly Gln Asp Thr Val Pro Glu Ser Thr
 1 5 10 15
 Ala Arg Met Gln Gly Ala Gly Lys Ala Leu His Glu Leu Leu Leu Ser
 20 25 30
 Ala Gln Arg Gln Gly Cys Leu Thr Ala Gly Val Tyr Glu Ser Ala Lys
 35 40 45
 Val Leu Asn Val Asp Pro Asp Asn Val Thr Phe Cys Val Leu Ala Ala
 50 55 60
 Gly Glu Glu Asp Glu Gly Asp Ile Ala Leu Gln Ile His Phe Thr Leu
 65 70 75 80
 Ile Gln Ala Phe Cys Cys Glu Asn Asp Ile Asp Ile Val Arg Val Gly
 85 90 95
 Asp Val Gln Arg Leu Ala Ala Ile Val Gly Ala Gly Glu Glu Ala Gly
 100 105 110
 Ala Pro Gly Asp Leu His Cys Ile Leu Ile Ser Asn Pro Asn Glu Asp
 115 120 125
 Ala Trp Lys Asp Pro Ala Leu Glu Lys Leu Ser Leu Phe Cys Glu Glu
 130 135 140
 Ser Arg Ser Val Asn Asp Trp Val Pro Ser Ile Thr Leu Pro Glu
 145 150 155

<210> 8
 <211> 165
 <212> PRT
 <213> Mus musculus

<220>
 <223> mouse growth arrest and DNA-damage-inducible
 protein (mGADD45)

<400> 8
 Met Thr Leu Glu Glu Phe Ser Ala Ala Glu Gln Lys Thr Glu Arg Met
 1 5 10 15
 Asp Thr Val Gly Asp Ala Leu Glu Glu Val Leu Ser Lys Ala Arg Ser
 20 25 30
 Gln Arg Thr Ile Thr Val Gly Val Tyr Glu Ala Ala Lys Leu Leu Asn
 35 40 45

Val Asp Pro Asp Asn Val Val Leu Cys Leu Leu Ala Ala Asp Glu Asp
 50 55 60
 Asp Asp Arg Asp Val Ala Leu Gln Ile His Phe Thr Leu Ile Arg Ala
 65 70 75 80
 Phe Cys Cys Glu Asn Asp Ile Asn Ile Leu Arg Val Ser Asn Pro Gly
 85 90 95
 Arg Leu Ala Glu Leu Leu Leu Leu Glu Asn Asp Ala Gly Pro Ala Glu
 100 105 110
 Ser Gly Gly Ala Ala Gln Thr Pro Asp Leu His Cys Val Leu Val Thr
 115 120 125
 Asn Pro His Ser Ser Gln Trp Lys Asp Pro Ala Leu Ser Gln Leu Ile
 130 135 140
 Cys Phe Cys Arg Glu Ser Arg Tyr Met Asp Gln Trp Val Pro Val Ile
 145 150 155 160
 Asn Leu Pro Glu Arg
 165

<210> 9
 <211> 165
 <212> PRT
 <213> Rattus norvegicus

<220>
 <223> rat growth arrest and DNA-damage-inducible protein
 (rGADD45)

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 20 25 30
 Gln Arg Thr Ile Thr Val Gly Val Tyr Glu Ala Ala Lys Leu Leu Asn
 35 40 45
 Val Asp Pro Asp Asn Val Val Leu Cys Leu Leu Ala Ala Asp Glu Asp
 50 55 60
 Asp Asp Arg Asp Val Ala Leu Gln Ile His Phe Thr Leu Ile Arg Ala
 65 70 75 80
 Phe Cys Cys Glu Asn Asp Ile Asn Ile Leu Arg Val Ser Asn Pro Gly
 85 90 95
 Arg Leu Ala Glu Leu Leu Leu Leu Glu Asn Asp Lys Ser Pro Ala Glu
 100 105 110
 Ser Gly Gly Leu Ala Gln Thr Pro Asp Leu His Cys Val Leu Val Thr
 115 120 125
 Asn Pro His Ser Ser Gln Trp Lys Asp Pro Ala Leu Ser Gln Leu Ile
 130 135 140

Cys Phe Cys Arg Glu Ser Arg Tyr Met Asp Gln Trp Val Pro Val Ile
 145 150 155 160

Asn Leu Pro Glu Arg
 165

<210> 10
 <211> 34
 <212> PRT
 <213> Homo sapiens

<220>
 <223> human GADD45 residues 58-91

<400> 10
 Leu Leu Ala Ala Asp Glu Asp Asp Asp Arg Asp Val Ala Leu Gln Ile
 1 5 10 15

His Phe Thr Leu Ile Gln Ala Phe Cys Cys Glu Asn Asp Ile Asn Ile
 20 25 30

Leu Arg

<210> 11
 <211> 34
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:human GADD45
 residues 58-91 with residues 62-67 changed to Ala
 by site-directed mutagenesis (M62-67)

<400> 11
 Leu Leu Ala Ala Ala Ala Ala Ala Ala Asp Val Ala Leu Gln Ile
 1 5 10 15

His Phe Thr Leu Ile Gln Ala Phe Cys Cys Glu Asn Asp Ile Asn Ile
 20 25 30

Leu Arg

<210> 12
 <211> 34
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:human GADD45
 residues 58-91 with residues 74-79 changed to Ala
 by site-directed mutagenesis (M74-79)

<400> 12
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 1 5 10 15

Ala Ala Ala Ala Ala Ala Ala Phe Cys Cys Glu Asn Asp Ile Asn Ile
 20 25 30

Leu Arg

<210> 13
 <211> 34
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:human GADD45
 residues 58-91 with residues 82-87 changed to Ala
 by site-directed mutagenesis (M82-87)

<400> 13
 Leu Leu Ala Ala Asp Glu Asp Asp Asp Arg Asp Val Ala Leu Gln Ile
 1 5 10 15

His Phe Thr Leu Ile Gln Ala Phe Ala Ala Ala Ala Ala Ala Asn Ile
 20 25 30

Leu Arg

<210> 14
 <211> 6
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<220>
 <223> Description of Artificial Sequence:Ran small
 nuclear GTPase carboxy-terminal domain closely
 related acidic motif

<400> 14
 Asp Glu Asp Asp Asp Leu
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<210> 15
 <211> 7
 <212> PRT
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<220>
 <223> Description of Artificial Sequence:GADD45 acidic
 motif residues 62-69

<400> 15
 Asp Glu Asp Asp Asp Arg Asp
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<210> 16
 <211> 46
 <212> PRT
 <213> Artificial Sequence

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<223> Description of Artificial Sequence:exemplary
peptide inhibiting GADD45-related dissociation of
Cdc2/cyclin B1 complexes

<400> 16

Glu Ala Ala Lys Leu Leu Asn Val Asp Pro Asp Asn Val Val Leu Cys
1 5 10 15

Leu Leu Ala Ala Asp Glu Asp Asp Asp Arg Asp Val Ala Leu Gln Ile
20 25 30

His Phe Thr Leu Ile Gln Ala Phe Cys Cys Glu Asn Asp Ile
35 40 45

<210> 17

<211> 38

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:exemplary
peptide inhibiting GADD45-related dissociation of
Cdc2/cyclin B1 complexes

<400> 17

Leu Leu Asn Val Asp Pro Asp Asn Val Val Leu Cys Leu Leu Ala Ala
1 5 10 15

Asp Glu Asp Asp Asp Arg Asp Val Ala Leu Gln Ile His Phe Thr Leu
20 25 30

Ile Gln Ala Phe Cys Cys
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<210> 18

<211> 26

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:exemplary
peptide inhibiting GADD45-related dissociation of
Cdc2/cyclin B1 complexes

<400> 18

Asp Asn Val Val Leu Cys Leu Leu Ala Ala Asp Glu Asp Asp Asp Arg
1 5 10 15

Asp Val Ala Leu Gln Ile His Phe Thr Leu
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<210> 19

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:exemplary
peptide inhibiting GADD45-related dissociation of
Cdc2/cyclin B1 complexes

<400> 19

Cys Leu Leu Ala Ala Asp Glu Asp Asp Arg Asp Val Ala Leu Gln
1 5 10 15

Ile His Phe Thr Leu
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<210> 20

<211> 21

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:exemplary
peptide inhibiting GADD45-related dissociation of
Cdc2/cyclin B1 complexes

<400> 20

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1 5 10 15

Asp Val Ala Leu Gln
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<210> 21

<211> 26

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:exemplary
peptide inhibiting GADD45-related dissociation of
Cdc2/cyclin B1 complexes

<400> 21

Glu Ala Ala Lys Leu Leu Asn Val Asp Pro Asp Asn Val Val Leu Cys
1 5 10 15

Leu Leu Ala Ala Asp Glu Asp Asp Arg
20 25

<210> 22

<211> 26

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:exemplary
peptide inhibiting GADD45-related dissociation of
Cdc2/cyclin B1 complexes

<400> 22

Asp Glu Asp Asp Asp Arg Asp Val Ala Leu Gln Ile His Phe Thr Leu
 1 5 10 15

Ile Gln Ala Phe Cys Cys Glu Asn Asp Ile
 20 25

<210> 23

<211> 27

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:exemplary
 peptide inhibiting GADD45-related dissociation of
 Cdc2/cyclin B1 complexes

<400> 23

Ala Asp Glu Asp Asp Asp Arg Asp Val Ala Leu Gln Ile His Phe Thr
 1 5 10 15

Leu Ile Gln Ala Phe Cys Cys Glu Asn Asp Ile
 20 25

<210> 24

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:exemplary
 peptide inhibiting GADD45-related dissociation of
 Cdc2/cyclin B1 complexes

<400> 24

Ala Asp Glu Asp Asp Asp Arg Asp Val Ala Leu Gln Ile His Phe Thr
 1 5 10 15

Leu

<210> 25

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence:exemplary
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 Cdc2/cyclin B1 complexes

<400> 25

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 1 5 10

<210> 26
 <211> 7
 <212> PRT
 <213> Artificial Sequence

<220>
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 peptide inhibiting GADD45-related dissociation of
 Cdc2/cyclin B1 complexes

<400> 26
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<210> 27
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 <212> PRT
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<220>
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 peptide inhibiting GADD45-related dissociation of
 Cdc2/cyclin B1 complexes

<400> 27
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 1 5 10 15

<210> 28
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
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 peptide inhibiting GADD45-related dissociation of
 Cdc2/cyclin B1 complexes

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<210> 29
 <211> 12
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence:exemplary
 peptide inhibiting GADD45-related dissociation of
 Cdc2/cyclin B1 complexes

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<210> 30
<211> 15
<212> PRT
<213> Artificial Sequence
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<220>
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Cdc2/cyclin B1 complexes

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1 5 10 15

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<212> PRT
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      peptide inhibiting GADD45-related dissociation of
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<400> 31
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1 5 10 15

Asp Val Ala Leu Gln Ile His Phe Thr Leu Ile Gln Ala Phe Cys Cys
20 25 30

Glu Asn Asp Ile
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<212> PRT
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<220>
<223> Description of Artificial Sequence:exemplary
peptide inhibiting GADD45-related dissociation of
Cdc2/cyclin B1 complexes

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Leu Asn Val Asp Pro Asp Asn Val Val Leu Cys Leu Leu Ala Ala Asp
1 5 10 15

Glu Asp Asp Asp Arg Asp Val Ala Leu Gln Ile His Phe Thr Leu Ile
20 25 30

Gln Ala Phe Cys Cys Glu Asn Asp Ile
35 40